

B

Abstract

Histopathologic Correlation between Chronic Hepatitis B and Nephropathy

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Backgrounds/Aims: The relationship between HBV infection and nephropathy has been reported with some differences according to the investigators and regions studied. Liver biopsies were not performed in most of the reports. In this study both liver and kidney biopsies were performed. The histologic correlation was analyzed between chronic B viral hepatitis and nephropathy. **Methods:** From January 1985 to June 2000, both liver and kidney biopsies were performed on 26 patients who had chronic hepatitis B, proteinuria, and hematuria. Also, a new histopathologic classification of chronic hepatitis was applied in the assessment of liver disease. **Result:** Light microscopy of kidneys showed IgA nephropathy in 7 cases (27%); minimal change nephrotic syndrome (MCNS) in 1 case (3.8%); and membranous glomerulonephritis (MGN) in 9 cases (34.6%), membranoproliferative glomerulonephritis (MPGN) in 9 cases (34.6%). Among the cases with a higher hepatitis activity index and fibrosis score, the frequency of MGN and MPGN was higher. The hepatitis activity index of cases with MGN was significantly higher than IgA nephropathy and MPGN ($p=0.011$, $p=0.039$). The fibrosis score of cases with MGN and MPGN was significantly higher than IgA nephropathy ($p=0.011$, $p=0.003$). The positivity of HBeAg was highest in cases with MGN. Serum C3 level was low in all cases but the serum C4 level was within normal range. Immunofluorescence studies showed granular deposition of IgG and C3 in the capillary loops in MGN. **Conclusion:** The frequency of MGN and MPGN was higher when the liver disease was more severe. It was suggested that HBeAg, IgG and C3 might contribute to the pathogenesis of MGN in HBsAg positive patients. (**Korean J Hepatol 2001;7: 413-422**)

Key Words: Hepatitis/Viral/Chronic Hepatitis B, Liver biopsy, Nephropathy, Renal biopsy

◇ 2001 9 3 ; 2001 10 12 ; 2001 10 30
◇ Abbreviations: ALT, Alanine transaminase; ANA, Anti-nuclear antibody; AST, Aspartate transaminase; C3, Complement 3; C4, Complement 4; GCW, Glomerular capillary wall; HBV, Hepatitis B virus; MCNS, Minimal change nephrotic syndrome; MES, Mesangium; MGN, Membranous glomerulonephritis; MPGN, Membranoproliferative glomerulonephritis; RF, Rheumatoid factor.

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2001

HBV

HBsAg

1990 5-10% 90 5%

0.2-1% 0.2%

HBV가

B (HBV) B

HBV

가

B

Henoch-Schönlein

HBV 26

HBsAg, HBeAg HBcAg

가

2.

1)

1968 De Groote⁹

HBV (chronic persistent hepatitis, (membranous CPH), (chronic active glomerulonephritis), (membrano-hepatitis, CAH)

(mesangial proliferative glomerulonephritis)

가

HCV , HBV

HBV

HBsAg

가

가

HBV

B

1

10

B

Table 1. New Histopathologic Classification of Chronic Hepatitis

Grading of chronic hepatitis		
Lobular activity		score
None	No necrosis	0
Minimal	Sinusoidal lymphocytosis	1
	+/- * 1 or less necrosis per 10 x objective field	
Mild	2-5 necrosis per 10 x objective field	2
Moderate	6-10 necrosis per 10 x objective field	3
Severe	More than 10 necrosis per 10 x objective field, or confluent necrosis (zone 3)	4
Porto-Periportal activity		score
None	< mild portal inflammation	0
Minimal	> mild portal inflammation	1
	+/- focal piecemeal necrosis in a few portal tract	
Mild	PMN [†] , focal in some or most portal tracts, or PMN < 50% in a few portal tracts	2
Moderate	PMN, around < 50% in most portal tracts, or PMN, around > 50% in a few or some portal tracts	3
Severe	PMN, around < 50% in most portal tracts / Septal surfaces, or bridging necrosis	4
Staging of chronic hepatitis		score
No fibrosis	Normal connective tissue	0
Portal fibrosis	Fibrous portal expansion	1
Periportal fibrosis	Periportal fibrosis with short septa extending into lobules or rare porto-portal septa (intact architecture)	2
Septal fibrosis	Fibrous septa reaching adjacent portal tracts and terminal hepatic venule (architectural distortion but no obvious cirrhosis)	3
Cirrhosis	Diffuse nodular formation	4

*, with or without; [†], piecemeal necrosis.

2)

IgA ,
(minimal change nephrotic syn- 4 .
drome), (membranous glomerulone- SPSS
phritis) (membranoproliferative (Window release 9.0) Package
glomerulonephritis) . 95% .

3.

B

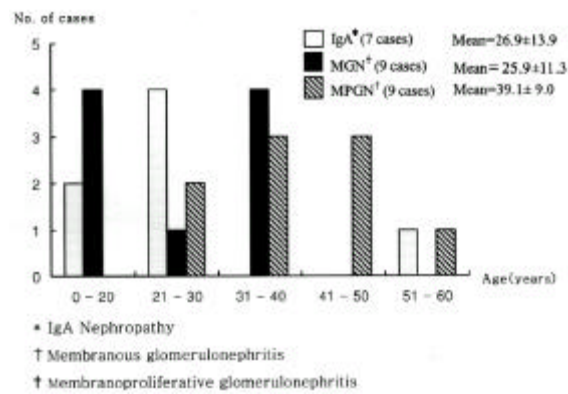
Mann-Whitney U-

1.

Table 2. Laboratory Findings in Patients with HBV-Associated Nephropathy at the Time of Biopsy

	IgA [*]	MCNS [†]	MGN [‡]	MPGN [§]	Total
Number of cases	7	1	9	9	26
Mean Age (Years)	27 ± 14	34	26 ± 11	39 ± 9	31 ± 12
Range (Age)	14-56	34	8-40	24-51	8-56
Sex (Male:Female)	4:3	1:0	8:1	8:1	21:5
Urine					
Proteinuria >3.5 g/day	4/7	1/1	5/7	4/7	14/22
Hematuria	7/7	1/1	9/9	9/9	26/26
Serum					
Increased AST/ALT (> 34 IU/L)	3/7	1/1	7/9	5/9	16/26
Decreased IgG (< 800 mg/dL)	3/6	1/1	2/9	3/7	9/23
Increased IgA (> 400 mg/dL)	2/6	0/1	0/9	2/7	4/23
Decreased C3 (< 90 mg/dL)	6/6	1/1	9/9	8/8	24/24
Decreased C4 (< 10 mg/dL)	0/6	0/1	0/9	0/8	0/24
HbsAg	7/7	1/1	9/9	9/9	26/26
HbeAg	4/7	0/1	8/9	5/9	17/26
Anti-HBs	0/7	0/1	0/9	0/9	0/26
Anti-Hbe	3/7	1/1	0/9	3/9	7/26
Anti-HBc	7/7	1/1	9/9	9/9	26/26
HBV-DNA	1/1	Not check	4/4	Not check	5/5

*, IgA Nephropathy; †, Minimal change nephrotic syndrome; ‡, Membranous glomerulonephritis; §, Membranoproliferative glomerulonephritis.

**Figure 1.** Age distribution.

1) B

26

27.0%, 1 3.8%, 7 3)

34.6% 가 가 .

2)

8 56

31.0 ± 12.3 가

21 , 5 4.2:1 .

1 가 34

25.9 ± 11.3

가 10 30

39.1 ± 9.0

가 30-40

가 , IgA 26.9 ± 13.9 20

(1).

Table 3. Immunofluorescent Findings in Patients with HBV-Associated Nephropathy

Nephropathy	No. of cases	Site of deposition	IgG	IgA	IgM	C3	C4	C1	Fibrinogen
IgA	7	GCW*	1	0	0	0	0	0	0
		Mes [†]	0	7	4	5	3	1	3
		GCW+Mes	0	0	0	1	0	0	0
MCNS	1	Mes	0	1	0	0	0	0	0
MGN	9	GCW	8	4	2	3	2	2	1
		Mes	0	0	0	1	0	1	0
		GCW+Mes	1	0	2	0	1	0	2
MPGN	9	GCW	2	2	2	2	3	2	1
		Mes	1	1	1	2	0	1	1
		GCW+Mes	0	1	1	1	1	0	0
Total	26		13	16	12	15	10	7	8

*, Glomerular capillary wall; [†], Mesangium.

가 26 (29.4%) 가 .

1 3.5g 가

14 44.4% . 14 IgA 2.

4 (28.6%), 1 3

(7.1%), 5 (35.7%),

4 (28.6%) . 26 16

AST ALT 가 가 . IgG,

IgA, IgM 23 IgG 9 .

971.6±539.7 mg/dL (IgG가 13 , IgA 16 , IgM 12 , C3 15 ,

800- 1600 mg/dL) . IgA 4 가 C4 10 , C1 7 , fibrinogen 8

299.8±213.0 mg/dL (70-400

mg/dL) , IgM 7 가 IgA

206.3±140.5 mg/dL (40- 250 mg/dL)

. C3, C4 24 C3 .

66.9±20.7 mg/dL (90- 180 mg/dL) IgA

, C4 25.7± IgA C3가 ,

10.7 mg/dL (10-40 mg/dL) IgA가

. ASO 가 17 IgG C3가 .

, RF 12 IgA C3가

2 가 . ANA 17 .

, anti-dsDNA 14

. LE cell 9 3. B

HBsAg 17 65.4% 17 26

IgA 4 (23.5%), 가 2 8 IgA

8 (47.1%) 5 5 62.5%, 3 37.5% .

Table 4. Histopathologic Characteristics of Nephropathy according to New Histopathologic Classification of Chronic Hepatitis B

Liver pathology		Renal pathology (No. of cases)				
Classification	Score	IgA	MCNS	MGN	MPGN	Total
Hepatitis activity index	0-2	5	0	0	3	8
	3-4	2	1	9	6	18
Fibrosis score	0-1	6	1	1	1	9
	2-4	1	0	8	8	17

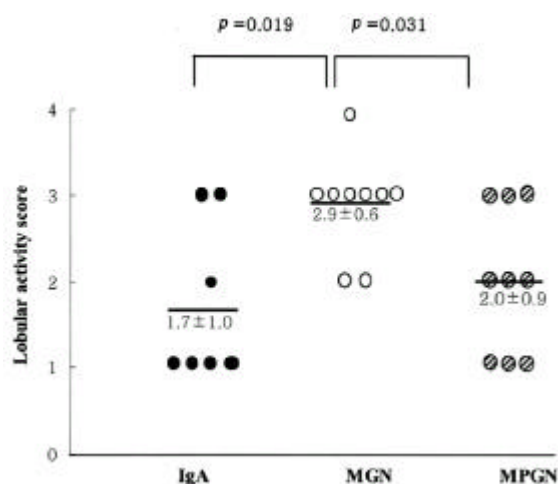


Figure 2. Lobular activity score according to histopathologic classification of nephropathy.

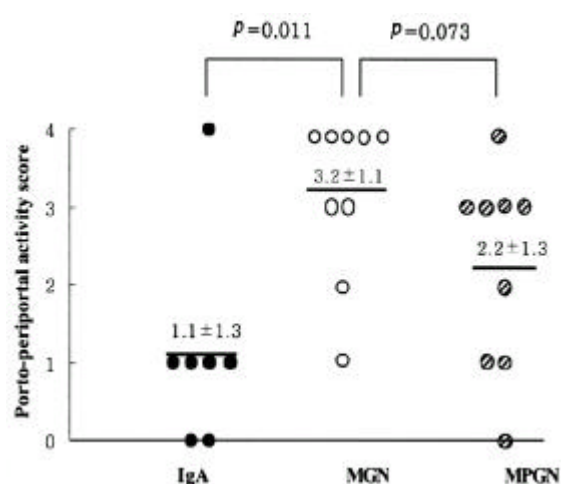


Figure 3. Porto-periportal activity score according to histopathologic classification of nephropathy.

가 3 18
IgA 2 11.1%,
1 5.6%, 9 50.0%,
6 33.3% . ,
1 9 IgA
6 66.7%, ,
1 11.1% .
2 17
IgA 1 5.8%,
8 47.1% (4).

4.

B

1.7 ± 1.0 , 2.9 ± 0.6 , 2.0 ± 0.9
IgA
가 (p = 0.019,
p = 0.031)(2).
2) /
/ 1.1 ± 1.3 , 3.2 ± 1.1 , 2.2 ± 1.3
IgA
가 (p = 0.011, p = 0.073)(3).

1)
26 가
IgA , ,
7 , 9 .
B

3)
/ 2.9 ± 2.1 , 6.1 ± 1.6 , 4.2 ± 2.1
IgA
가 (p = 0.011,
p = 0.039)(4).

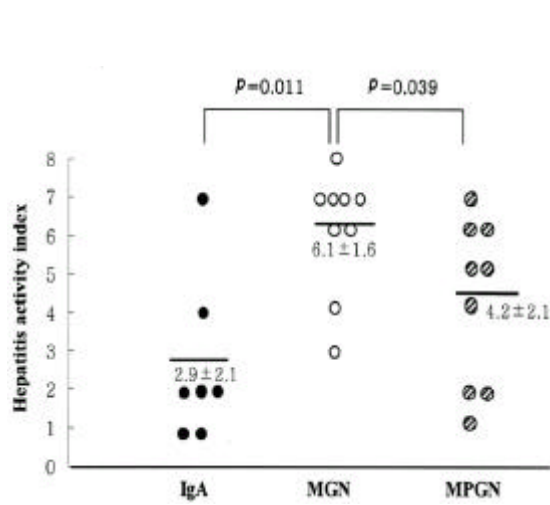


Figure 4. Hepatitis activity index according to histopathologic classification of nephropathy.

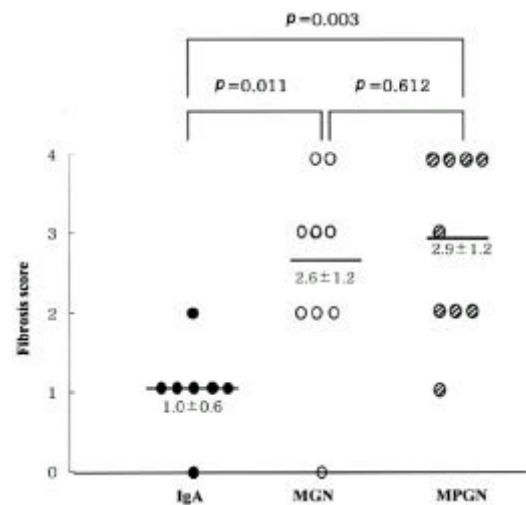


Figure 5. Fibrosis score according to histopathologic classification of nephropathy.

4) 가 IgA , , , 1.0 ± 0.6 , 2.6 ± 1.2 , 2.9 ± 1.2 가 IgA 가 (p=0.011, p=0.003)(5).

. Vos¹³ 9.8% 20.3%, Nagy¹⁴ 0.99% 13%, La¹⁵ 4.2% 31.7% ,¹⁶ 9.4% 25.3%,¹⁷ 12.3% 17.1% HBV가 B 가 .

5 Combes¹¹ 1971 15 33 B 가 12 , 2 가 4 ,¹⁸ 39 B 가 . Morzycka¹² , , 20 가 . HBsAg 55 28 , 16 , 44 4 HBV (membranous glomerulonephritis), (membranoproliferative glomerulonephritis), (mesangial proliferative glomerulonephritis) 가 , HBV⁵ ,^{6,7} 가 .

B 3

. Lai ¹⁹ 74 HBsAg , 21 ,
 25 가 5 4 ,
 IgA 18 , 1 가 1
 11 , (minimal
 change nephrotic syndrome) 4 . Bhimma . ⁵ B ,
²⁰ 93 HBsAg 1
 70 , 6 , 5 4
 (focal segmental glomeru- , 1 가
 losclerosis) 5 , 5 가
 . ²¹ 87 HBsAg
 29 가 . 26
 18 , IgA 16 .
 . ⁵ 33 HBsAg 26
 13 가 가
 (minimal change nephrotic syndrome) 9 ,
 6 , 5 가 가
 . ¹⁸ 39 HBsAg Amemiya ²³ , B
 25 , 9 ,
 3 , HBsAg HBeAg , HBeAg
 2 . 26 , HBsAg
 9
 가 가 . IgA 7 . HBeAg 10 daltons
 (27.0%) 가 IgA , HBeAg-Ab 100 daltons
 HBV IgA HBsAg-Ab 200 daltons
 . , HBV
 IgA HBsAg
 가
 . , HBeAg
 HBsAg , HBsAg
 .
 HBeAg 17 65.4%
 가 가 . 8 (47.1%) 가
 . HBeAg
 B . , C3
 B 24 C4
 . Knieser ²² Wiggelinkhuizen ⁶

12 . B

C3가 16 12 , HBsAg
C4 9 1 .

IgA B 가
Iida ²⁴ IgA , HBeAg
130 HBsAg 4 C3가
(3.1%) 4 1 HBeAg IgG C3
4 HBeAg, IgG

HBsAg HBeAg C3
HBsAg, HBeAg IgA 가
IgA .

Nagy ¹⁴ 가 HBsAg 0.99%
IgA HBsAg 가
16% HBsAg
31% . ,
Lai ²⁵ 122 IgA 17.2%
HBsAg : B
HBsAg

HBsAg HBcAg HBV
HBV가 IgA ,
²⁶ B
736 IgA B
66 9% ²¹ 87 . ,
HBsAg IgA 16
(17%) . HBV
26 7 (27%) 가 . : 1985
IgA C3 2000 6
가

26 B
²⁶ 26
 , : 26 31.0±
B 25.9±11.3 , 12.3 4.2 : 1 .
41.3±13.5 26 가
 , 39.1 14 . B
±9.0 32.5±14.5 26 IgA 7 (27.0%),
1 (3.8%), 9 (34.6%)
B 9 (34.6%) .
 , HBeAg 가
가 .

HBeAg 17 IgA 4
(23.5%), 8 (47.1%)
5 (29.4%)
가 .
(hepatitis activity index)
가 IgA
가
(p=0.011, p=0.039).
IgA
가 (p=0.011,
p=0.003). C3 24
C4
IgG C3가
IgA C3가
B
가
가
가
HBeAg
, C3가
IgG C3
HBeAg, IgG C3
B , , ,

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